A PHASE I STUDY OF AUTOLOGOUS HUMAN INTERLEUKIN 2 (IL-2) GENE MODIFIED TUMOR CELLS IN PATIENTS WITH REFRACTORY METASTATIC OVARIAN CANCER

NON-TECHNICAL ABSTRACT

No systemic therapy improves survival for refractory metastatic ovarian cancer that has failed platinum and taxol based therapies. Interest in immunotherapy using gene therapy for ovarian cancer has been stimulated by the findings that cytokine transduced tumor vaccines can induce anti tumor immune responses. We have conducted extensive laboratory studies using a strategy for inducing anti-tumor immune responses to non-immunogenic tumors including ovarian cancer. By inserting immunostimulatory genes into rodent tumor cells, and injecting them under the skin, systemic anti tumor immune responses have been reproducibly induced, resulting in eradication of small amounts of implanted tumor at distant sites. The interleukin 2 (IL-2) gene in these model studies conferred potent anti tumor effects compared to other cytokines tested. Efficient introduction of this gene in the model cancer vaccine cells was accomplished with retroviral vectors and with non viral delivery methods including liposomes and DNA. This efficiency made feasible the generation of genetically engineered human ovarian cancer vaccines from individual patients. Using a non viral pMP6-IL-2 vector, we are able to prepare ovarian cancer cell vaccines from over 80% cases in clinical trial simulations. The genetically engineered ovarian cancer cells then secrete IL-2 in the range that confers anti tumor efficacy.

Lethal irradiation of the genetically engineered ovarian cancer cells did not diminish therapeutic effects genetically engineered to secrete the IL-2 gene in pre clinical studies. Irradiation of genetically modified tumor cells affords a measure of safety for human studies without compromising potential therapeutic efficacy. The identical approach is currently under ongoing phase I study in NIH-RAC approved protocol # 9403-086 for breast cancer. To develop this new strategy for the treatment of ovarian cancer, the safety of active immunotherapy produced by this procedure must also be established in a phase I (toxicity) study.

The overall objective of the phase I portion of the study is to evaluate the safety and tolerability of active immunotherapy of IL-2 gene modified ovarian cancer cell injections using cells derived from a patient's ovarian cancer cells. To help ensure safety, all tumor cells will be irradiated prior to injection. It is unlikely that the injections will benefit patients enrolled in the phase I portion of the trial with advanced tumor burdens of metastatic disease.